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Faculty Spotlight: Gordon Gribble

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Image courtesy of the Gribble Group

BY SAM REED '19

Figure 1: Dr. Gordon Gribble (right) is an esteemed Organic Chemistry Professor, role model, and mentor. This picture was taken at the 2002 Goldschmidt Conference in Davos, Switzerland.

Faculty Spotlight:

Dr. Gordon Gribble

Professor of Chemistry

Professor Gordon Gribble received his B.S. from U.C. Berkeley and his Ph.D. from the University of Oregon. He has been at Dartmouth for the past 49 years, and in that time he has taught chemistry to a great number of students. His research in the field of organic chemistry features indole and triterpenoid synthesis, and has yielded a wide range of medications.

Why organic chemistry as opposed to a different field of chemistry?

It all goes back to 1951 when I was 10 years old. I got a chemistry set for Christmas and, I remember, I was working with my dad in the kitchen, doing experiments. I really loved the idea of making something new, noticing how chemicals react to form colors, smoke, things like that. In fact, I was making firecrackers and sparklers later on when I was maybe 12-14.

So you really budded early then?

I was very interested in chemistry. In those days you could actually go to a chemistry store and buy things like concentrated sulfuric acid. I remember my mother taking me to J.T. Baker Chemical Company in San Francisco and buying a concentrated bottle of sulfuric acid, which you could never do today, of course.

How do you think organic chemistry can advance fields of public health in ways that other fields of chemistry cannot?

Well organic chemistry, of course, is the chemistry of carbon compounds. All pharmaceuticals, all new drugs, almost all new materials, are based on carbon. Carbon is the central element in organic chemistry, of course.

I know that a lot of your work has to do with indoles. What can this work do for the field of chemistry?

Well indol is a heterocyclic, two-ring system that is in everything we eat. It's in tryptophan. It's in serotonin - our brain chemical. It's in pharmaceuticals, and has many biological applications. All migraine drugs, for example (and that's just one example), contain the indole core, and indole is a ubiquitous compound, as I mentioned. It's in lots of pharmaceuticals and materials. Nature uses the indole ring to make a myriad of natural products.

I'll ask you the same question about triterpenoids.

Triterpenoids are in everything we eat also, although they don't contain nitrogen. They're biosynthesized from acetic acid, actually - which is something we eat – but they're in things like cranberries, pokeberries, really all plant material contains some triterpenoids. Ursolic acid is a common one in cranberries. Oleanolic acid common in leaves to make our potential drug, is in olive oil, for example. And in rosemary, that's another biological source.

When you're beginning your research, do you think of a problem you want to solve and then devise a structure, or do you create a novel structure, and then see how it can be used?

A combination of that. With the triterpenoid that we invented in 1998, we started with the premise that triterpenoids in plants have some biological activity, some anti-inflammatory activity, some anti-cancer activity. Probably not sufficient enough to be used in the clinic, to be used as a drug. Folk medicine reports uses of things like oleanolic acid, ursolic acid, to treat various diseases, but it's really not sufficient to be used. So we had the idea, if you take one of these compounds – we chose two: oleanolic acid and ursolic acid. Chemically, we started to modify those compounds to see if we could amplify the biological activity. The 151st compound we synthesized, its called CDDO, was actually four thousand times more active than oleanolic acid, the starting materials. It's a ten-step synthesis that took three years to accomplish, going from the stuff we get from olive oil to a compound that made it through phase three of clinical trials, after phase 1 and phase 2 trials for cancer and chronic kidney disease.

So does a lot of your research still revolve around this triterpenoid, and if not, what does it consist of?

Right now I'm writing a new paper on a derivative of CDDO that we think will be better than the original CDDO, which is now called a bardoxolone methyl. We synthesized bardoxolone methyl in my laboratory in 1998, published it in 2000. We have a better synthesis reported a couple years ago, which actually reduces the number of synthetic steps in half. But the new compound, where we've made a compound having 1 less methyl group on what's called the "A-ring," has activity that's about 10 times better than bardoxolone methyl. So we're very excited about that new compound.

But as you know, I'm retiring from teaching in August, and my research might go another two years or so but after that I'll probably be out of the laboratory completely.

That's a great bridge to my next question. Over the course of your career so far, what are the biggest ways your research has been impacted by your students?

Well Dartmouth students are incredibly intelligent, enthusiastic, and motivated, by-and-large. So that's tremendous feedback that I receive when I work with undergraduates, and graduates, and post-docs as well. So that's been a real joy with me; not only doing research with them but also teaching them.

Any advice for a budding organic chemist?

Work a little bit all the time, keep on top of things, and if you're into research as an undergraduate, you went to work with a professor and mentors in the laboratory. It's a matter of dedication and falling in love with what you're doing in the laboratory, as I did a long time ago. D